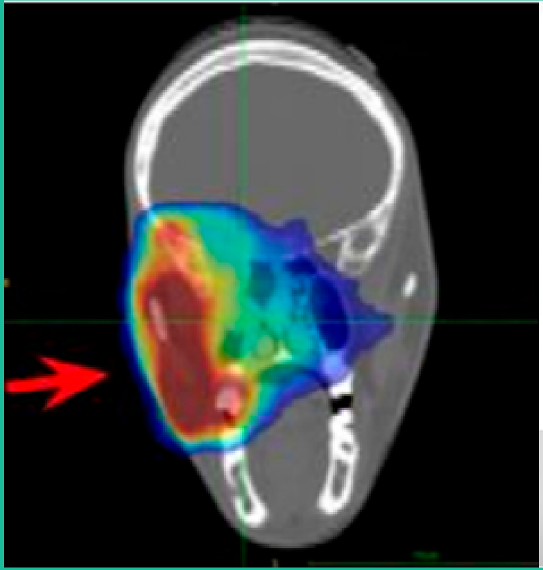

1: Introduzione alla radioterapia

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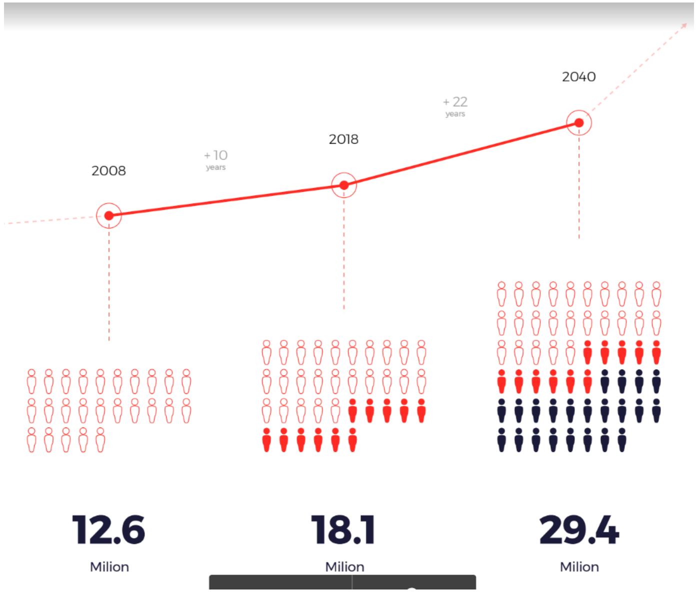
30/04/2024

What is radiotherapy

From Wikipedia:

Radiation therapy or **radiotherapy**, often abbreviated **RT**, **RTx**, or **XRT**, is a therapy using ionizing radiation, generally provided as part of cancer treatment to control or kill malignant cells and normally delivered by a linear accelerator. Radiation therapy may be curative in a number of types of cancer if they are localized to one area of the body. It may also be used as part of adjuvant therapy, to prevent tumor recurrence after surgery to remove a primary malignant tumor (for example, early stages of breast cancer). Radiation therapy is synergistic with chemotherapy, and has been used before, during, and after chemotherapy in susceptible cancers. The subspecialty of oncology concerned with radiotherapy is called radiation oncology. A physician who practices in this subspecialty is a radiation oncologist.

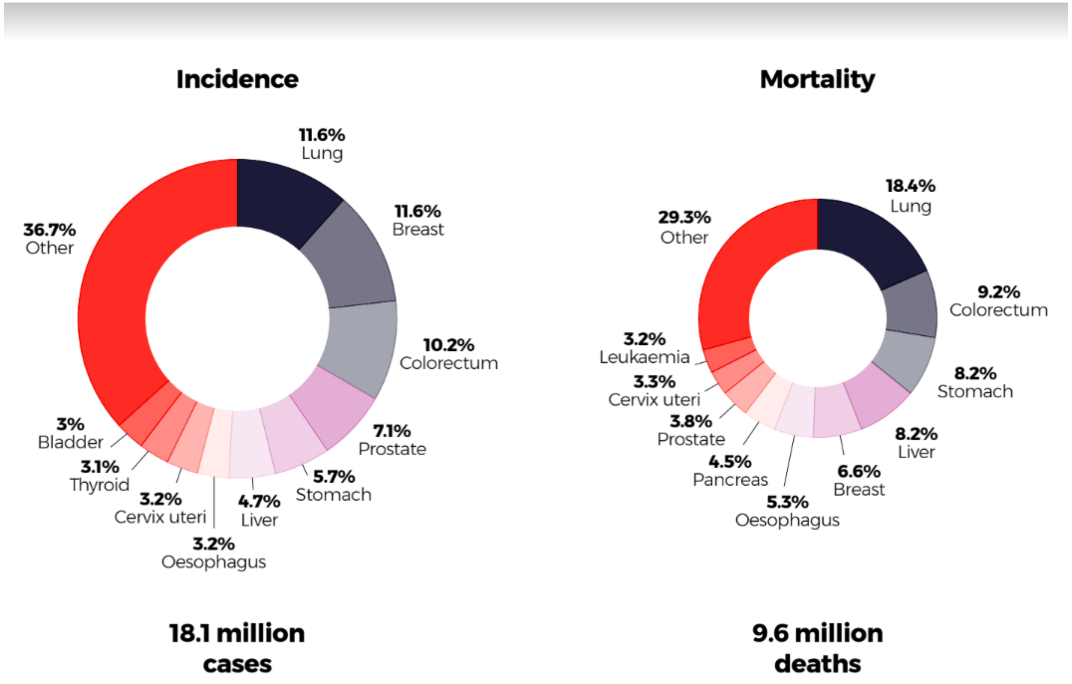
Global burden of cancer



Estimated global burden of cancer in 2018 and that in 2040, from WHO cancer report 2020. (WHO in Italian is usually referred as OMS)

- In 2018, there were an estimated 18 million new cases of cancer and 10 million deaths from cancer worldwide
- The predicted global burden will double to about 29–37 million new cancer cases by 2040
- Of the 15 million deaths between the ages of 30 and 69 (“premature deaths”) in 2018, 4.5 million were due to cancer

Some stats about cancer



Distribution of cases and deaths by the leading 10 cancer types in 2018 for both sexes. from WHO cancer report 2020

- Different techniques to treat cancer:
  -surgery, chemotherapy, radiotherapy and immunotherapy
- Surgery is the most widespread treatment approach for cure of solid tumours
- About 2/3 patients diagnosed with cancer receive **curative** or **palliative** radiation treatments

Fundamental variables: Fluence

Fluence:

- Defined as the number of particles in a beam
- In beam line design, particles travel almost in the same direction (few mrad of aperture), it is sufficient to use a plane element of area and define the fluence as

  $\Phi = dN/dA$;

- Where dA is an infinitesimal element of area perpendicular to the beam and dN is the number of particles passing through
- Units: Number of particles/cm^2
- The **fluence rate** is: $\dot{\Phi} \equiv \frac{d\Phi}{dt}$; Number of particles /cm^2 s

Fundamental variables: (absorbed) dose

Absorbed dose: **dE/dm**
where dE is the energy deposited in dm matter by ionizing radiation

- **The deposited energy is the incident energy minus the energy leaving the mass minus the energy released in nuclear transformations (to keep the dose from becoming negative when the mass contains a radioactive source).**

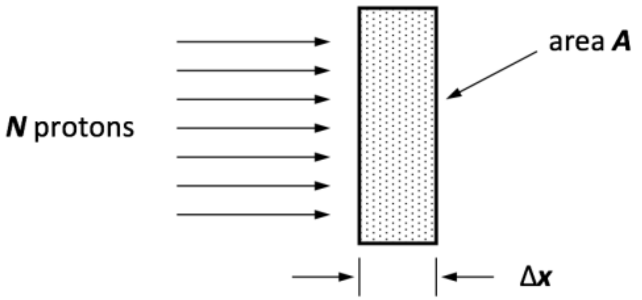
- The medium should always be specified

- Unit of measurement:
  Gray (Gy), defined as 1 joule of energy absorbed per Kg of matter
  1 Gy=1 J/Kg

Fundamental variables: (absorbed) dose

- The absorbed dose is equal to the radiation exposure (ions or C/kg) of the radiation beam multiplied by the ionization energy of the medium to be ionized.
- E.g.: 1 roentgen would deposit $8.76*10^{-3}$ Gy in air
- The equation relating dose to fluence and stopping power:

$$D \equiv \frac{\text{energy}}{\text{mass}} = \frac{(dE/dx) \times \Delta x \times N}{\rho \times A \times \Delta x} = \Phi \frac{S}{\rho}$$



- **Dose=Fluence*mass stopping power**

- **Typical dose values for radiotherapy treatments: 20-70 Gy depending on the type, size of tumour (e.g. Solid tumour~60-70 Gy, lymphoma~20-40 Gy)**

Questions:
Is the absorbed dose sufficient to characterize the incident radiation for radiotherapy purposes?

Tips:
Remember prof. Veronese’s last couple of lessons

Fundamental variables: equivalent dose

- In order to evaluate the probability of of cancer induction and other long time scale effects, the type of radiation and the sensitivity of the irradiated tissues plays an important role
- The absorbed dose is a physical measurable quantity that do not take into account the biological effects (remember slide 8)
- The **Equivalent dose H_T** is derived from the absorbed dose as: $$H_T = \sum_R W_R \cdot D_{T,R}$$

  -$D_{T,R}$ absorbed dose in Gy in tissue T by radiation type R
  -W_R weighting factor that depends on beam type/energy
- It represents the possibility of radiation induced cancer or damage taking into account both physical quantities (Dose) and relative biological effectiveness of the radiation (W_R)
- Unit of measuremet in SI: Sievert (Sv), since W_R is a weight factor, Sv=J/Kg, or in CGS: roentgen equivalent man (rem), 1 rem=0.01 Sv
- Commonly used in dosimetry and radiation protection field

Fundamental variables: equivalent dose

Table 1. A comparison of existing w_R values and those proposed to the ICRP

Type and energy range of incident radiation		Radiation weighting factor (w_R)	
		Publication 60	Proposed[c]
Photons, all energies		1	1
Electrons and muons (all energies)[a]		1	1
Protons (incident)		5	2
Neutrons, energy	< 10 keV	5	Use the proposed w_R function in Fig. 1 below
	10 keV–100 keV	10	
	> 100 keV–2 MeV	20	
	> 2 MeV–20 MeV	10	
	> 20 MeV	5	
Alpha particles, fission fragments, and heavy ions[b]		20	20[d]

ICRP Publication 92

Relative Biological Effectiveness (RBE), Quality Factor (Q), and Radiation Weighting Factor (wR)

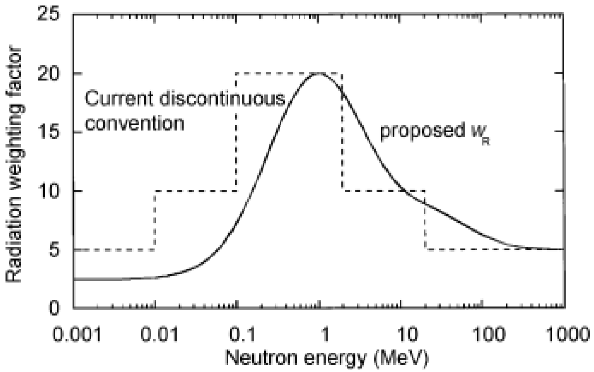


Fig. 1. The radiation weighting factor w_R for neutrons introduced in *Publication 60* (ICRP, 1991) as a discontinuous function of the neutron energy (- - -) and the proposed modification (—).

Fundamental variables: effective dose

- In order to take into account also the radiobiological effectiveness of the human tissue:
- The **Effective dose E** is derived as:

Calculating from the equivalent dose:

$$E = \sum_T W_T \cdot H_T = \sum_T W_T \sum_R W_R \cdot \bar{D}_{T,R}.$$

Calculating from the absorbed dose:

$$E = \sum_T W_T \sum_R W_R \cdot \frac{\int_T D_R(x,y,z)\rho(x,y,z)dV}{\int_T \rho(x,y,z)dV}$$

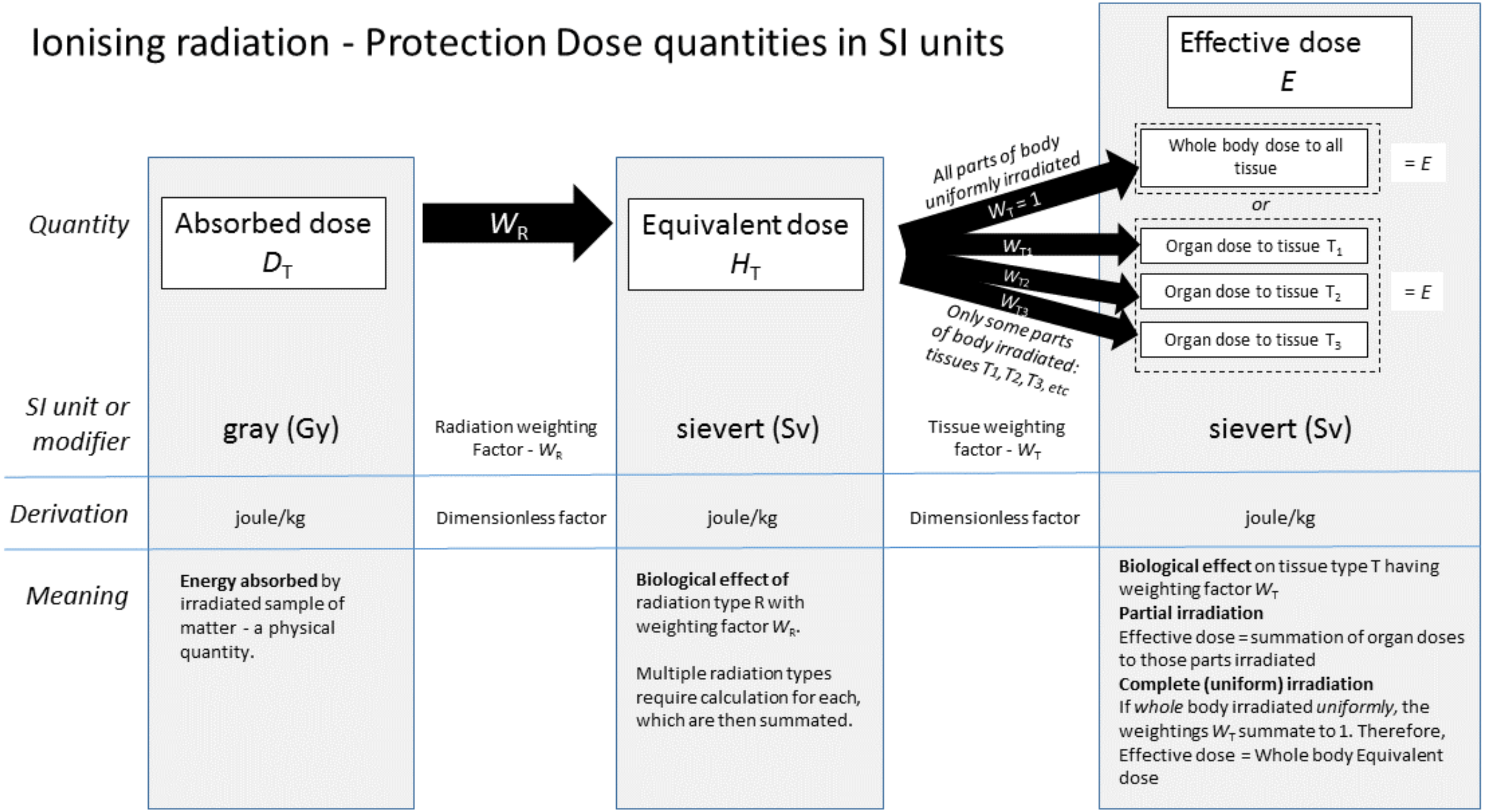
Where

E is the effective dose to the entire organism
H_T is the equivalent dose absorbed by tissue T
W_T is the tissue weighting factor defined by regulation
W_R is the radiation weighting factor defined by regulation
$\bar{D}_{T,R}$ is the mass-averaged absorbed dose in tissue T by radiation type R
$D_R(x,y,z)$ is the absorbed dose from radiation type R as a function of location
$\rho(x,y,z)$ is the density as a function of location
V is volume
T is the tissue or organ of interest

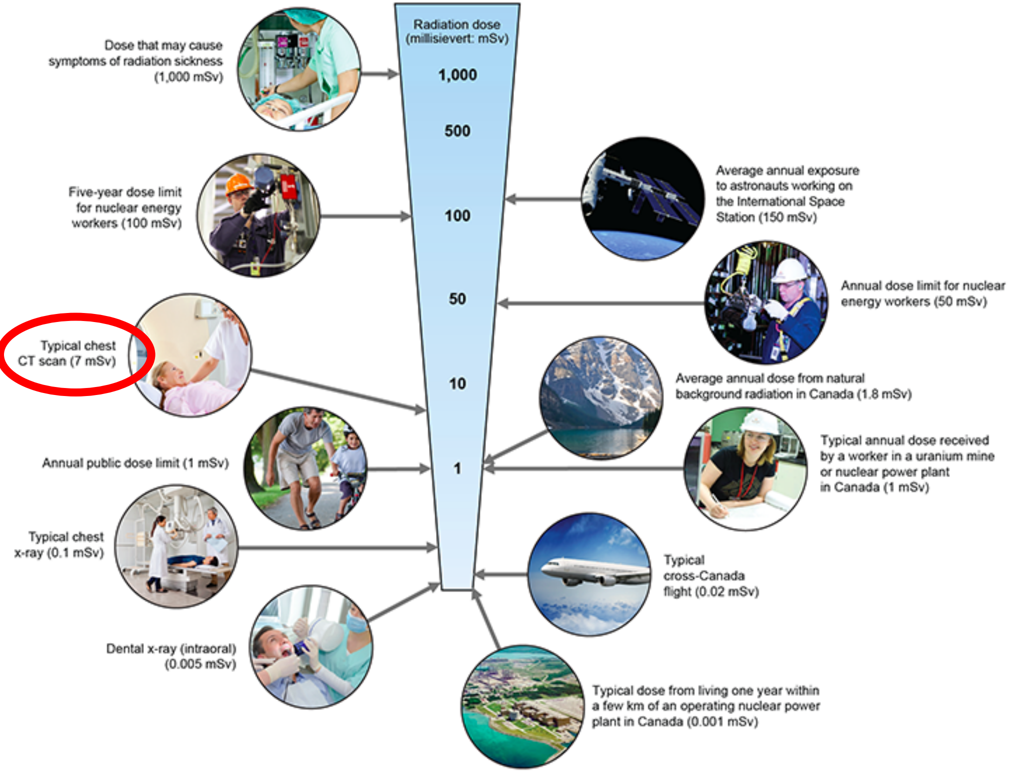
Weighting factors for different tissues[12]

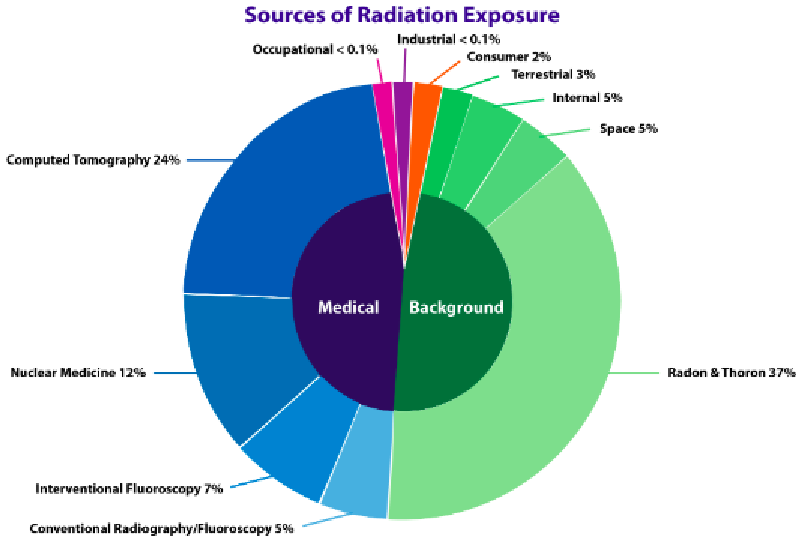
Organs	Tissue weighting factors		
	ICRP26 1977	ICRP60 1990[13]	ICRP103 2007[14]
Gonads	0.25	0.20	0.08
Red Bone Marrow	0.12	0.12	0.12
Colon	–	0.12	0.12
Lung	0.12	0.12	0.12
Stomach	–	0.12	0.12
Breasts	0.15	0.05	0.12
Bladder	–	0.05	0.04
Liver	–	0.05	0.04
Oesophagus	–	0.05	0.04
Thyroid	0.03	0.05	0.04
Skin	–	0.01	0.01
Bone surface	0.03	0.01	0.01
Salivary glands	–	–	0.01
Brain	–	–	0.01
Remainder of body	0.30	0.05	0.12
Total	**1.00**	**1.00**	**1.00**

Fundamental variables: dose summary



Background radiation





Average Annual Radiation Dose

Sources	Radon & Thoron	Computed Tomography	Nuclear Medicine	Interventional Fluoroscopy	Space	Conventional Radiography/ Fluoroscopy	Internal	Terrestrial	Consumer	Occupational	Industrial
Units mrem (United States) mSv (International)	228 mrem 2.28 mSv	147 mrem 1.47 mSv	77 mrem 0.77 mSv	43 mrem 0.43 mSv	33 mrem 0.33 mSv	33 mrem 0.33mSv	29 mrem 0.29 mSv	21 mrem 0.21 mSv	13 mrem 0.13 mSv	0.5 mrem 0.005 mSv	0.3 mrem 0.003 mSv

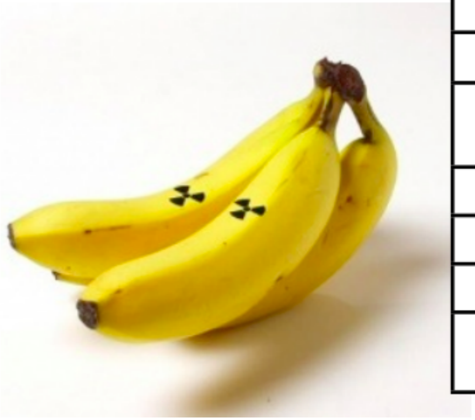
(Source: National Council on Radiation Protection & Measurements, Report No. 160)

Background radiation

Banana Equivalent Dose

Bananas are a natural source of radioactive isotopes.

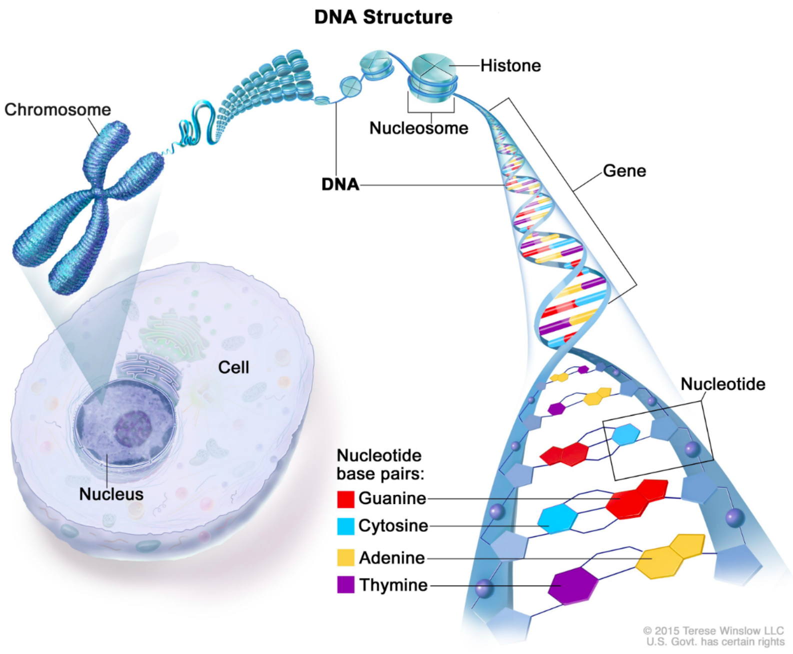
Eating one banana = 1 BED = 0.1 μSv = 0.01 mrem



Number of bananas	Equivalent exposure
100,000,000	Fatal dose (death within 2 weeks)
20,000,000	Typical targeted dose used in radiotherapy (one session)
70,000	Chest CT scan
20,000	Mammogram (single exposure)
200 - 1000	Chest X-ray
700	Living in a stone, brick or concrete building for one year
400	Flight from London to New York
100	Average daily background dose
50	Dental X-ray
1 - 100	Yearly dose from living near a nuclear power station

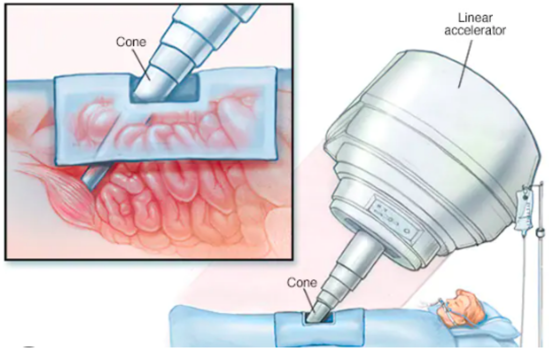
Radiotherapy

to induce biological damage in cancer cells and avoid their proliferation



- First radiotherapy treatment in ~ **1900**
- Discovery of DNA in 1953
- The DNA encodes the genetic instructions used in the growth, development, functioning and reproduction of the cells
- **The target of radiation is the DNA**

Types of radiotherapy



Mainly two types of radiotherapy:

- Conventional radiotherapy with photons
- Particle therapy with hadrons (mainly protons and ^{12}C ions)
- There are also other less “common” form of radiotherapy (e.g.: IORT, VHEE etc.)

Radiotherapy can be use for:

- Therapeutic treatments to cure or reduce the metastasis
- As palliative care to reduce the pain for people with a serious illness

Dose response

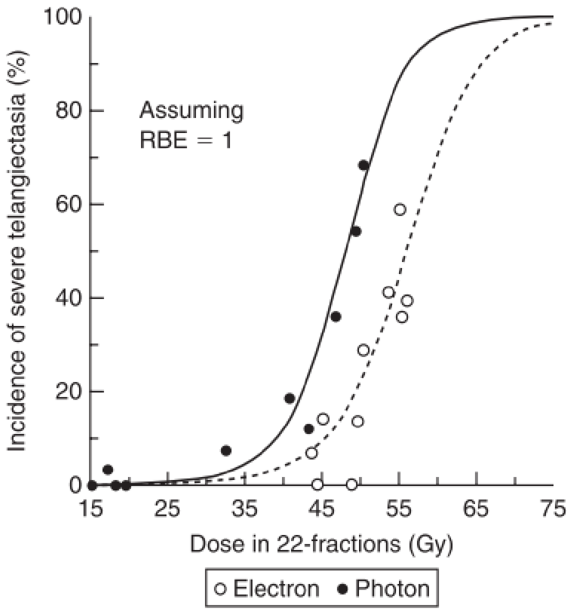


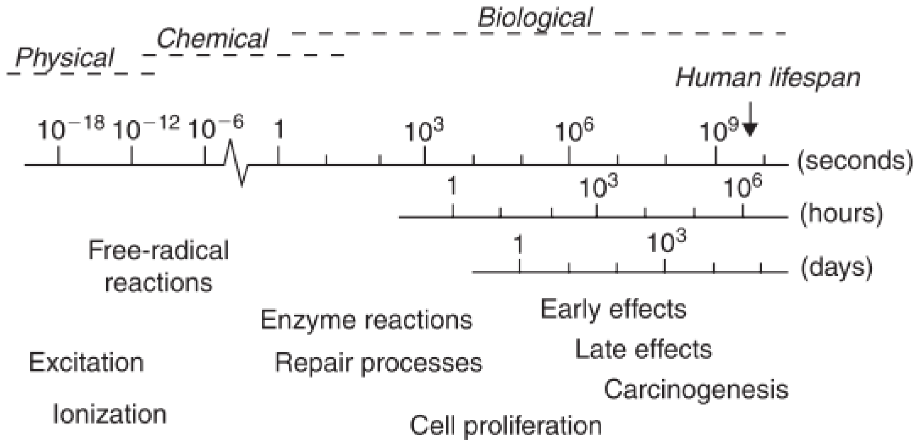
Figure 5.1 Examples of dose–response relationships in clinical radiotherapy. Data are shown on the incidence of severe telangiectasia following electron or photon irradiation. RBE, relative biological effectiveness. From Bentzen and Overgaard (1991), with permission.

- Clinical radiobiology is concerned with the relationship between a given physical absorbed dose and the resulting biological response and with the factors that influence this relationship

- **There is no dose below which the complication rate is zero: there is no clear-cut limit of tolerance**

- **Radiation dose–response curves have a sigmoid (i.e. 'S') shape that can be fitted with different models**

Radiation time scale



Irradiation of any biological system generates a succession of processes that differ enormously in time-scale

- **Physical phase:** consists of interactions between charged particles and the atoms of the tissue
- **Chemical phase**: the damaged atoms and molecules react with other cellular components in rapid chemical reactions
- **Biological phase:** all the subsequent processes. e.g.: DNA repaired, early/late effects ect.

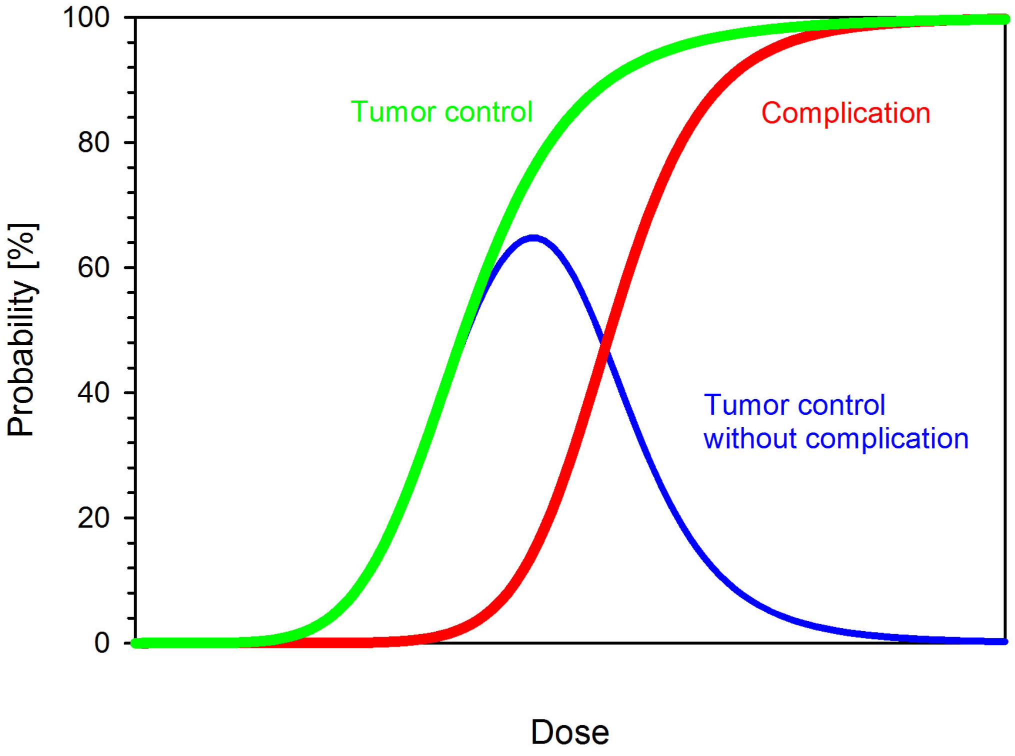
Radiation response of normal and tumour tissues

- The response of a tumour is seen by **regression**, often followed by **regrowth**
- **Local control** of a tumor: the total disappearance of the primary tumor and neighboring lymph node metastases without any local recurrence on long-term follow-up
- The responses of normal tissues to therapeutic radiation exposure range from those that cause mild discomfort to others that are life-threatening
- The speed at which a response develops varies widely from one tissue to another and often depends on the dose of radiation that the tissue receives.
  (e.g.: radiation damage on epithelial tissues in weeks, connective tissues in months/years)

Toxicity

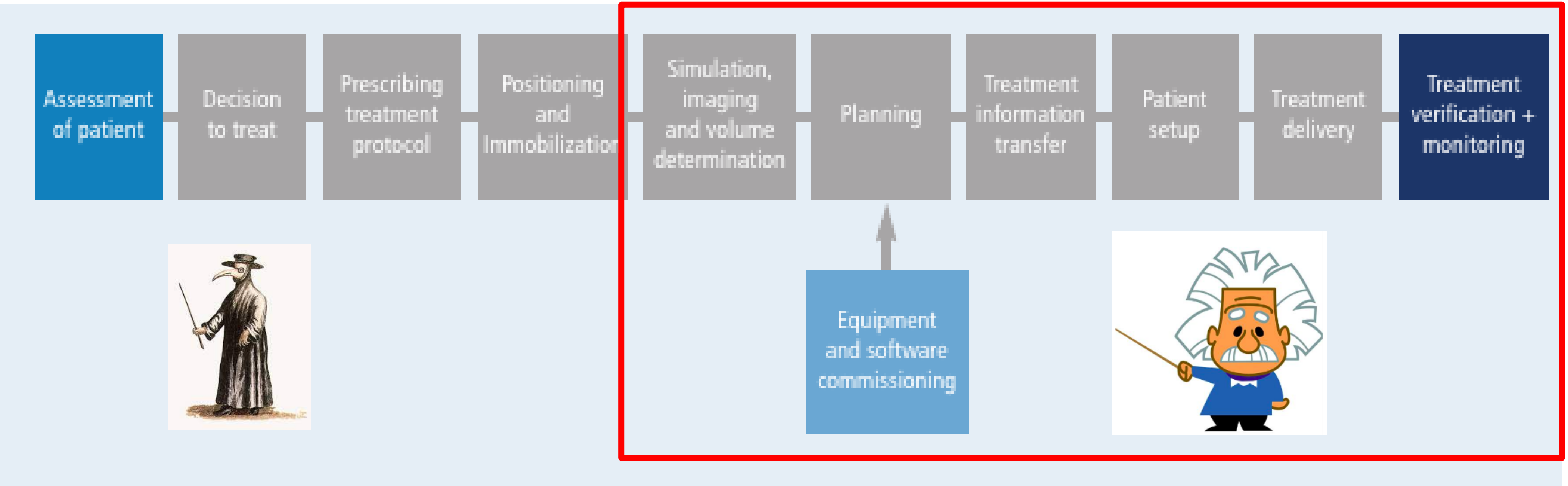
- Two types of toxicity due to radiotherapy: acute and long term toxicity
  -Systemic symptoms: Fatigue, local skin reaction, oropharyngeal mucositis
  -Long-term sequelae: may occur many months or years after irradiation
- The long-term (years) effects are the most difficult to evaluate.
  It is not possible to retrieve the specific cause of a cancer or disease
- The risk of radiation-induced second cancers is much greater in young and very young cancer patients. Increased cancer rates may persist life-long.
- Most radiation-induced second cancers occur in organs and tissues in the high-dose volume but some may also appear in the low dose (?2Gy) volume
- Radiation therapy is known to be mutagenic, carcinogenic, teratogenic, with increased risk of developing both secondary leukemia and solid tumour
- There are different biological mechanisms leading to second cancers after radiotherapy, depending on dose distribution and age of the irradiated patient. The dose–risk relationship is unlikely to follow a simple mathematical function

Goal of radiotherapy



- **Radiotherapy as a trade-off between tumor control and normal tissue complication probability**
- **The goal of radiotherapy is to maximize the tumor control curve, minimizing the normal tissue complication effects**
- Using different techniques, particles etc., the therapeutic window of a radiation therapy can be extended

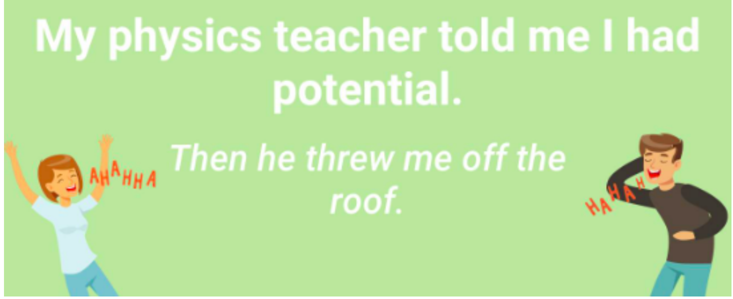
Stages of radiotherapy treatment



From WHO radiotherapy risk profile

Questions?
Or comments?

Scientificast



Per capire il motivo di questa “barza brutta” bisogna ascoltare il podcast **scientificast**